| **Supplemental Digital Content 2.** Summary statistics by age group for open-ring metabolite PK parameters from Study BPR-PIP-002 derived using non-compartmental methods (4 groups) |
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| PK Parameter | Infants (3 months – 1 year)20 mg/kg IV over 4 hours | Children (2 – 5 years)20 mg/kg IV over 2 hours | Children (6 – 11 years)15 mg/kg IV over 2 hours | Adolescents (12 – 17 years)10 mg/kg IV over 2 hours |
| N | Mean (CV%)Median (Min – Max) | N | Mean (CV%)Median (Min – Max) | N | Mean (CV%)Median (Min – Max) | N | Mean (CV%)Median (Min – Max) |
| Cmax (μg/mL) | 1 | 2.49 (―)2.49 (2.49 – 2.49) | 14 | 1.30 (68.5%)1.07 (0.228 – 3.38) | 6 | 1.38 (61.5%)1.62 (0.222 – 2.43) | 8 | 1.13 (18.9%)1.11 (0.886 – 1.53) |
| Tmax (h) | 1 | 4.07 (―)4.07 (4.07 – 4.07) | 14 | 2.88 (79.7%)2.03 (0 – 8.08) | 6 | 3.18 (84.1%)2.03 (1.80 – 7.95) | 8 | 2.28 (74.1%)2.05 (0 – 6.08) |
| AUC0-last (μg•h/mL) | 1 | 14.7 (―)14.7 (14.7 – 14.7) | 14 | 5.03 (78.3%)4.47 (0.601 – 15.5) | 6 | 5.25 (63.5%)6.69 (0.828 – 8.64) | 8 | 4.65 (23.2%)4.50 (3.55 – 6.35) |
| AUC0-tau (μg•h/mL) | 1 | 14.7 (―)14.7 (14.7 – 14.7) | 14 | 5.03 (78.3%)4.47 (0.601 – 15.5) | 6 | 5.25 (63.5%)6.69 (0.828 – 8.64) | 8 | 4.65 (23.2%)4.50 (3.55 – 6.35) |
| T1/2 (h) | 1 | ― | 14 | 3.62 (25.5%)3.64 (2.70 – 5.22) | 6 | 3.30 (35.3%)2.67 (2.59 – 4.65) | 8 | 3.78 (45.8%)3.35 (2.00 – 7.47) |
| CLSS (L/h/kg) | 1 | 1.08 (―)1.08 (1.08 – 1.08) | 14 | 6.52 (106%)3.58 (1.04 – 26.6) | 6 | 3.86 (102%)1.79 (1.15 – 10.5) | 8 | 1.68 (27.7%)1.70 (1.04 – 2.25) |
| VSS (L/kg) | 1 | 3.59 (―)3.59 (3.59 – 3.59) | 14 | 24.8 (136%)13.1 (3.81 – 130) | 6 | 19.7 (146%)6.46 (3.91 – 70.7) | 8 | 6.06 (25.8%)6.26 (4.22 – 7.87) |
| Raccumulation | 1 | ― | 14 | 1.28 (10.9%)1.28 (1.15 – 1.53) | 6 | 1.24 (14.2%)1.14 (1.13 – 1.44) | 8 | 1.31 (20.8%)1.24 (1.07 – 1.91) |
| Note: AUC0-last, area under the plasma concentration-time curve from time zero to the last measured concentration; AUC0-tau, area under the plasma concentration-time curve from time zero to tau; CLSS, oral clearance at steady state; Cmax, maximum plasma concentration; CV%, percent coefficient of variation; h, hours; IV, intravenous(ly); L, liters; Max, maximum; Min, minimum; mL, milliliters; μg, micrograms; N, number of observations or subjects; Raccumulation, accumulation ratio; T1/2, half-life; Tmax, time at which maximum concentration occurs; VSS, volume of distribution at steady state.1. Note that AUC0-tau is identical to AUC0-last for all patients as the time of the last observed concentration was within +/- 15 minutes of 8 hours in each patient.
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